The current management of spinal cord cavernoma

Velz, Julia ; Bozinov, Oliver ; Sarnthein, Johannes ; Regli, Luca ; Bellut, David

Abstract: BACKGROUND Spinal cavernous malformations (SCM) were once thought to be rare lesions of the spinal cord. However, with the broad use of modern imaging techniques the incidence of SCM has significantly increased over the last decades. Management of both symptomatic and incidental findings is therefore of growing importance. However, experience with treatment and follow-up is very limited. METHODS We performed a single institution retrospective review of consecutive patients with SCM treated at our Department between 2006-2016 and discuss the clinical features as well as surgical versus conservative outcomes. We further provide a systematic literature search and discuss the best management of SCM, analyzing recent publications on SCM imaging techniques, surgical approaches and natural history. RESULTS From a total number of 406 consecutive patients with cavernous malformations (CM) treated at our Department between 2006-2016, 29 (7.1 %) were found to be affected by SCM. The localization was cervical in 10 (34.5 %), cervicothoracic in 3 (10.4 %) and thoracic in 16 (55.2 %) patients. In 90 % of patients (n = 26) the diagnosis was made after onset of clinical symptoms. Conservative management was performed for 8 patients, whereas 21 patients underwent surgical removal of the lesion via a posterior approach using (hemi-) laminectomy or laminoplasty. Functional status improved in 15 patients (62. 5%) and remained unchanged in 6 patients (28.5 %) in the operative group, whereas 2 patients (25 %) improved and 6 patients (75 %) remained unchanged in the conservative group during long-term follow-up. CONCLUSIONS Gross-total resection is the only definitive treatment option for symptomatic SCM. Surgical extirpation of the symptomatic SCM lesion through an unilateral laminectomy (= hemilaminectomy) approach within 3 months of presentation seems to be good treatment option with an acceptable risk of complications and good long-term outcomes. Conservative treatment should be performed in asymptomatic patients and seems to be an option as well in elderly patients and if patients' symptoms at diagnosis are mild and do not show progression over time.

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ORIGINAL ARTICLE

The current management of spinal cord cavernoma

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ABSTRACT

BACKGROUND: Spinal cavernous malformations (SCM) were once thought to be rare lesions of the spinal cord. However, with the broad use of modern imaging techniques the incidence of SCM has significantly increased over the last decades. Management of both symptomatic and incidental findings is therefore of growing importance. However, experience with treatment and follow-up is very limited.
METHODS: We performed a single institution retrospective review of consecutive patients with SCM treated at our Department between 2006-2016 and discuss the clinical features as well as surgical *versus* conservative outcomes. We further provide a systematic literature search and discuss the best management of SCM, analyzing recent publications on SCM imaging techniques, surgical approaches and natural history.
RESULTS: From a total number of 406 consecutive patients with cavernous malformations (CM) treated at our Department between 2006-2016, 29 (7.1%) were found to be affected by SCM. The localization was cervical in 10 (34.5%), cervicothoracic in 3 (10.4%) and thoracic in 16 (55.2%) patients. In 90% of patients (N.=26) the diagnosis was made after onset of clinical symptoms. Conservative management was performed for 8 patients, whereas 21 patients underwent surgical removal of the lesion via a posterior approach using (hemi-) laminectomy or laminoplasty. Functional status improved in 15 patients (62.5%) and remained unchanged in 6 patients (28.5%) in the operative group, whereas 2 patients (25%) improved and 6 patients (75%) remained unchanged in the conservative group during long-term follow-up.
CONCLUSIONS: Gross-total resection is the only definitive treatment option for symptomatic SCM. Surgical extirpation of the symptomatic SCM lesion through an unilateral laminectomy (=hemilaminectomy) approach within 3 months of presentation seems to be good treatment option with an acceptable risk of complications and good long-term outcomes. Conservative treatment should be performed in asymptomatic patients and seems to be an option as well in elderly patients and if patients' symptoms at diagnosis are mild and do not show progression over time.

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Key words: Spinal cord cavernoma - Congenital abnormalities - Therapeutics.

Spinal cavernous malformations (SCM) were once thought to be rare entities and previously accounted for only 5% of intramedullary spinal cord tumors.[1] Nevertheless, since the broad use of modern imaging techniques such as high resolution magnetic resonance imaging (MRI) of the spine for evaluation of degenerative conditions or other spinal pathologies, especially the rising number of incidental findings has led to a significantly increasing incidence of SCM.[2] To date, SCM account for up to 20% of intramedullary spinal cord tumors.[2] The mean age at presentation is in the fourth decade.[3, 4] Clinical presentation is distinct and varies from slow, progressive decline of neurological symptoms to acute onset of neurological deficits with severe paresis in asymptomatic young patients without any prior warning.[5, 6] As many as 40% of patients with SCM, may harbor cranial cavernous malformation (CCM).[7, 8]

Management of both symptomatic but especially less or asymptomatic SCM is therefore of growing importance. However, existing evidence in terms of treatment and follow-up is limited mostly to retrospective studies and therefore biased (Table I).[3, 4, 9-19] According to the literature gross-total resection is the only definitive treatment option for symptomatic SCM, but surgery in this highly el-

Table I.—*Overview of published series >20 patients with SCM and clinical management (operative* vs. *conservative).*

Authors	Study design	Total N.	Mean age	M	F	Spinal level	Treatment	
							Conservative	Surgical
Jallo *et al.*,[3] 2006	Retrospective	26	38	17	9	Cervical 8; cervicothoracic 1, thoracic 7	0	26
Labaugê *et al.*,[9] 2008	Retrospective	53	40.2	26	27	Cervical 12, thoracic 14	13	40
Lu *et al.*,[10] 2010	Retrospective	22	42	12	9	Cervical 6; thoracic 16	0	22
Steiger *et al.*,[11] 2010	Retrospective	20	39.2	9	11	Cervical 7, cervicothoracic 1, thoracic 11, lumbar 1	3	17
Choi *et al.*,[12] 2011	Retrospective	21	39.3	8	13	Cervical 10, thoracic 9, thoracolumbar 1, lumbar 1	0	21
Liang *et al.*,[13] 2011	Retrospective	96	34.5	60	36	Cervical 25, thoracic 68, lumbar 3	16	81
Mitha *et al.*,[14] 2011	Retrospective	80	39.9	38	42	Cervical 46, thoracic 68, conus medullaris 6	0	80
Tong *et al.*,[15] 2012	Retrospective	20	33.9	15	5	Cervical 9, cervicothoracic 4, thoracic 7	0	20
Wachter *et al.*, 2012 [16]	Retrospective	30	42	13	17	Cervical 10, cervicothoracic 1, thoracic 13	0	30
Badhiwala *et al.*, 2014 [4]	Retrospective	24	40.3	14	10	Cervical 10, cervicothoracic 1, thoracic 13	13	11
Reitz *et al.*, 2015 [17]	Retrospective	48	41.3	25	23	Cervical (39.5 %), Thoracic (56.3 %), thoracolumbar (4.2 %)	0	48
Ardeshiri *et al.*, 2016 [18]	Retrospective	25	46.0	14	11	Cervical/cervicothoracic 11, thoracic/thoracolumbar 14	5	20
Imagama *et al.*, 2017 [19]	Prospective	41	39.0	18	23	Cervical 17, thoracic 24	0	41
Present cases	Retrospective	29	44.6	13	16	Cervical 10, cervicothoracic 3, thoracic 16	8	21

oquent tissue seems to display a significant risk of morbidity. Due to advances in surgical techniques and tools such as intraoperative imaging and neuromonitoring the surgical removal of SCM became much safer.[20-24] Nevertheless up to date, only few larger mono-institutional series that allow for analysis of operative strategies and outcome in patients with SCM exist.[3, 4, 9-13, 16-18, 25] The largest study so far includes 96 patients in a retrospective data collection. So far only one prospective trial has been carried out and available (Table I).[19]

Materials and methods

Patient population

In the present study, we retrospectively identified all patients with cavernous malformation (CM) that were treated at the Department of Neurosurgery at the University of Zurich between 2006-2016. Patients with radiological or histological diagnosis of at least one SCM were included in the data collection. All radiological and histopathological diagnosis of SCM were confirmed by a senior neuroradiologists or neuropathologists.

Patients' characteristics

The patients' past medical history was analyzed and age, gender, clinical symptoms, date of and symptoms at diagnosis, surgical procedures, date of and symptoms at last follow-up were noted. Patients' neurological state was classified according to the Frankel Scale.[26] A) complete loss of motor and sensory function below the level of lesion; B) sensory function only below the level of lesion; C) preserved motor non-functional below the level of the lesion; D) useful, but abnormal motor function below the level of lesion; and E) no clinically detected abnormalities in sensory or motor function — abnormal reflexes or subject and subjective sensory abnormalities may be present (Table II). Neurological status at diagnosis was graded based on Frankel grade in the conservative group. In the

Table II.—*Frankel Classification grading system.*

Grade A	Complete neurological injury: no motor or sensory function clinically detected below the level of injury
Grade B	Preserved sensation only: no motor function clinically detected below the level of the injury; sensory function remains below the level of the injury but may include only partial function
Grade C	Preserved motor non-functional: some motor function observed below the level of the injury, but is of no practical use to the patient
Grade D	Preserved motor function: useful motor function below the level of the injury; patient can move lower limbs and walk with or without aid, but does not have a normal gait or strength in all motor groups.
Grade E	Normal motor: no clinically detected abnormality in motor or sensory function with normal sphincter function; abnormal reflexes and subjective sensory abnormalities may be present

surgical group Frankel Score was determined in the preoperative course and before discharge (=postoperative course). Data of repeated magnetic resonance imaging (MRI) was available for all included patients. T1 (with and without contrast enhancement), T2 and especially gradient echo sequences (GRE) in all three planes (axial and sagittal) or susceptibility-weighted imaging (SWI) was routinely performed in all patients. MRI was analyzed in regard to exact localization of CM within the spine and the spinal cord and size. Changes of configuration and size during follow-up was noted as well.

Follow-up

Neurological status was graded based on Frankel grade in all patients during first follow-up 3-6 months after surgery (operative cohort) respectively after diagnosis (conservative cohort). The patient's clinical status, resolution of pain, and any additional and related surgical procedures that the patient may have undergone by the time of follow-up were noted.

Overall outcome was determined during long-term follow-up in our outpatient clinic and categorized as de-

Table III.—*Clinical characteristics, surgical approaches and outcome in our operative group (=21 patients with SCM). Frankel Grade was determined at the day of hospitalization (=preoperative), the day at discharge (=postoperative) and during short-time follow-up (3-6 m) in our outpatient clinic. Overall outcome was determined during long-term follow-up (mean 3.2 [±0.58] years per patient) in our outpatient clinic and categorized as declined, unchanged and improved.*

Case #	Age (years, sex)	Spinal level	Involved segments	Bleeding/ acute symptoms	Duration of symptoms before surgery	Surgical approach	IONM/ ioUS/ ioMRI or ioCT	Complete resection	Frankel Score			Overall outcome (long-term FU)
									Preop	Postop	Short-time FU (3-6 m)	
1	19, F	T 9	1	Y	3 d	Left unilateral laminectomy T 9	x/Y/N	Y	A	B	D	Improved
2	30, F	C7-T1	2	Y	7 d	Right unilateral laminectomy C7 +T 1	Y/Y/ ioMRI	Y	D	D	D	Unchanged
3	32, F	C1-C2	2	N	6 m	Right unilateral laminectomy C2	Y/x/N	Y	E	D	D	Unchanged
4	44, M	T11	1	N	18 d	Laminoplasty T 11	Y/Y/ioCT	Y	D	D	E	Improved
5	75, M	T11-12	2	Y	7 w	Laminectomy T 11 + T 12	x/x/x	Y	D	D	D	Unchanged
6	37, M	T10	1	N	4 m (+ 4y ago)	Right unilateral laminectomy T 9 + T 10	x/x/N	N/Reoperation	D	D	D	Improved
7	27, M	T2	1	N	2 m	Laminoplasty T 2	Y/Y/N	Y	D	D	E	Improved
8	82, M	C3-C4	2	N	2 w (+ 2y)	Laminectomy C3/C4	Y/x/N	Y	C	C	C	Improved
9	26, M	C4	1	N	3 m	Left unilateral lamincetomy C4	Y/Y/N	Y	E	E	E	Unchanged
10	64, F	C8	1	N	5 y	Left unilateral lamincetomy C8	Y/Y/N	Y	D	D	D	Unchanged
11	65, F	T4	1	N	7 y	Right unilateral lamincetomy C4 + C5	Y/x/N	Y	D	D	D	Improved
12	32; F	C3-C4	2	N	1 m	Left unilateral lamincetomy C3 + C4	Y/Y/N	N	D	D	E	Improved
13	38, F	T6	1	N	3 w	Right unilateral lamincetomy C6 + C7	Y/Y/N	Y	D	D	D	Improved
14	29, M	T2	1	N	3 m	Left unilateral lamincetomy T 2	Y/Y/N	Y	D	D	D	Improved
15	68, F	T2-T3	2	N	6 m	Left unilateral lamincetomy T 2 + T 3	Y/Y/N	Y	D	D	D	Improved
16	59, F	T12	1	Y	7 d	Laminoplasty T 11 + T 12	Y/Y/N	Y	C	D	E	Improved
17	26, F	C1-C2	2	Y	2 d	Laminectomy C1 + Lamiotomie C2	Y/Y/N	N/reoperation	D	D	D	Unchanged
18	20, F	T2-T3	2	N	4 m	Laminoplasty T 2 + T 3	Y/Y/N	Y	D	C	D	Improved
19	14, M	C4	1	None	None	Laminoplasty C3-C5	Y/Y/N	Y	E	D	E	Improved
20	46, F	C2-C3	2	N	8 m	Right unilateral lamincetomy C3	Y/Y/N	Y	D	D	E	Improved
21	48, M	T6-T7	2	N	9 m	Laminectomy T 6+ T 7	x/N/N	Y	D	D	E	Improved

F: female; M: male; C: cervical; T: thoracal; Y: yes; N: no; x: no data available; IONM: Intraoperative neuromonitoring; ioUS: intraoperative ultrasound; ioMRI: intraoperative MRI; ioCT: intraoperative computer tomography; preop: preoperative; postop: postoperative; FU: follow-up.

TABLE IV.—*Clinical characteristics and outcome in our non-operative group (=8 patients with SCM). Frankel Grade was determined at the day of diagnosis and during short-time follow-up (3-6 m) in our outpatient clinic. Overall outcome was determined during long-term follow-up (mean 3.2 [±0.58] years per patient) in our outpatient clinic and categorized as declined, unchanged and improved.*

Case #.	Age (years, sex)	Spinal level	Involved segments	Acute symptoms	Duration symptoms/ first consultation	Neurological status/Frankl Score		Overall outcome (long-term FU)
						Date of diagnosis	Short-term FU (3-6 m)	
1	57, M	T 12	2	Y	6 d	D	E	Improved
2	46, M	C7-T1	2	N	3 y	E	E	Unchanged
3	39, F	C5-C6	2	N	9 m	E	E	Improved
4	42, F	T11	1	None	-	E	E	Unchanged
5	47, M	T2	1	Y	5 d	D	D	Unchanged
6	26, F	C7; T6	2	None	-	E	E	Unchanged
7	79, M	C3-C4	2	N	1 d	E	E	Unchanged
8	77, F	T11	1	Y	5 d	C	C	Unchanged

F: female; M: male; C: cervical; T: thoracal; Y: yes; N: no; none: no neurological symptoms; FU: follow-up.

clined, unchanged and improved. Information was obtained through notes from the last postoperative clinic visit (Tables III, IV).

Literature review

We undertook a systematic literature search. We searched PubMed in English language with the MeSH terms "cavernous malformation," "cavernoma," "cavernous hemangioma," "cavernous angioma," "angiographically occult vascular malformation," cross-matched with terms pertinent to the CNS location (that is, intramedullary, spine, spinal cord) in various combinations. We obtained the full-text version for all studies we considered relevant. To identify additional resources, we manually searched references of articles with potential relevance.

The present study was approved by the Cantonal Ethics Committee (KEK-ZH; application number 2017-00330).

Results

Patient population

From 1st January 2006 to 31st December 2016, 406 patients with CM were treated at the Department of Neurosurgery at the University of Zurich; 29 (7.1%) of these patients harbored a SCM and were included in the present study. The clinical characteristics of the individual patients are summarized in Tables III, IV. The mean patient age in our patient cohort was 44.6 years (range 13.8-81.5 years). There was a slight female dominance (N.=16, 55.2%). The location of the CM within the spine was cervical in 10 (34.5%), cervicothoracic in 3 (10.4%) and thoracic in 16 patients (55.2%). The diagnosis was made in 89.7% of patients (N.=26) after the sudden onset or progression of significant clinical symptoms. Three patients presented without focal neurological deficits (10.3%). Two patients in our series also had multiple intracranial CM. The remaining patients had a single spinal pathology and no known family history of CM. The mean long-term follow-up was 3.2 (±0.58) years per patient (range 0.4-10.4 years). The total follow-up time was 110.3 person-years.

Initial clinical presentation and mechanisms

Twenty-six patients (89.7%) in our study cohort were symptomatic at diagnosis -10 patients (34.5%) showed acute onset of clinical signs and neurological deficits, whereas 16 patients (55.2%) displayed progressive neurological deficits due to SCM rebleeding and chronic progressive spinal cord compression. The most common presenting symptoms were sensory deficits (75.7%), paresis (65.5%) and bladder dysfunction (42.1%). Other commonly observed symptoms were gait disturbances and dysesthesia. Multiple neurological deficits occurred in 18 patients (62.1%). In 3 patients (10.3%) incidental finding in MRI led to the diagnosis of SCM. At the time of diagnosis one patient showed complete loss of motor and sensory function below the level of the SCM lesion (Frankel grade A); 3 patients presented with severe paraparesis and loss of functional strength (grade C), 17 patients had useful, but abnormal motor function below the level of injury (grade D) and 8 patients showed no clinically detected abnormalities in sensory or motor function and were in Grade E according to the Frankel classification (Tables III, IV).

Magnetic resonance imaging

MRI findings of all patients were consistent with SCM. Figure 1 shows a representative case with mixed signal intensity on T1-weighted images, whereas microhemorrhages and hemosiderin deposits cause a low-signal-intensity ring surrounding the SCM on T1- and T2-weighted images.

Operation and pathological findings

All 21 surgically treated patients underwent a posterior approach using (hemi-) laminectomy or laminoplasty with intended gross-total resection of the cavernoma-suspected lesion. We preferred an unilateral approach by an extended interlaminar fenestration or unilateral laminectomy for SCM reaching the spinal cord surface on one side, whereas in midline lesions a laminectomy or laminoplasty was carried out. Unilateral laminectomy was performed in 12 patients: one segment in 6 and two segments in 6 cases, 4 patients underwent laminectomy and in 5 patients laminoplasty with reinsertion and fixation of the laminae was performed. Nine patients were treated using a classic median myelotomy due to a deep-seated median lesion. A paramedian approach to a superficial lesion was performed in 12 patients. Complete microsurgical resection of the lesion was achieved in 18 of the 21 (85.7%) surgically treated patients. Two patients underwent re-operation due to residual SCM. Time point of surgery was ≤1 week in 5 patients, >1 week and less than ≤3 months in 8 patients and >3 months in 8 patients after onset of symptoms. The intraoperative findings for all 21 patients were uniform, with its mulberry-like appearance surrounded by hemosiderin deposits and gliosis (Figure 2).[27] Histopathology revealed in all cases a circumscribed thin walled vascular sinusoids lined by a thin endothelium and an adventitial layer devoid of a medial layer. The surrounding tissue was stained with hemosiderin and in gliotic in reaction to the blood products (Figure 3). Figure 4 shows a representative case with preoperative, intraoperative and MRI during short-time follow-up.

Intraoperative ultrasound assistance

Ultrasound Imaging was performed using high-frequency probes — data was available for 15 out of 21 operated patients. Before dural opening, ultrasound imaging was

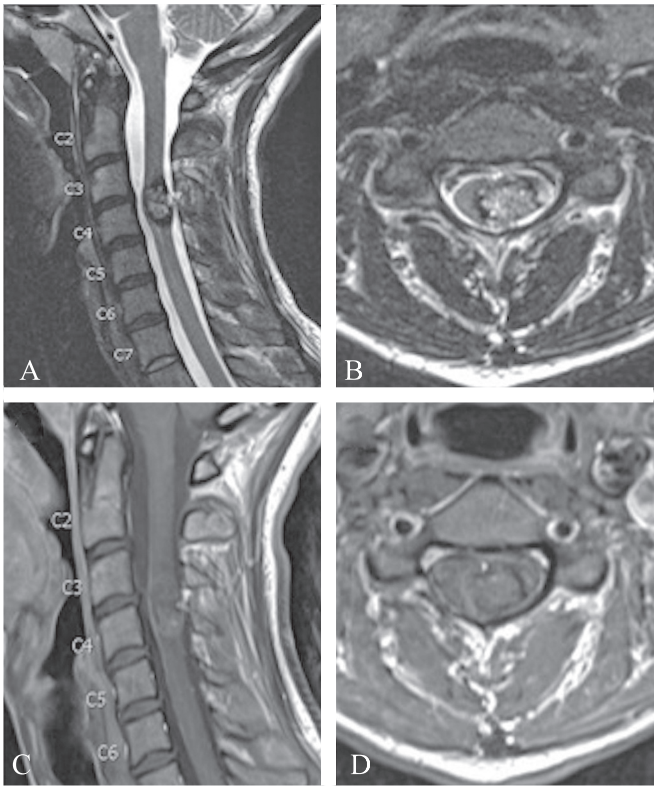

Figure 1.—32-year-old women with an SCM at the level of C3-C4 (case #12; operative group) sagittal (A) and axial (B) native T2-weighted MRI showing a pathognomic hyperintense lesion surrounded by a hypointense hemosiderin rim after hemorrhage. Sagittal (C) and axial (D) T1-weighted MRI. The patient presented with a history of thoracolumbar pain and motor deficit of her left arm for one month.

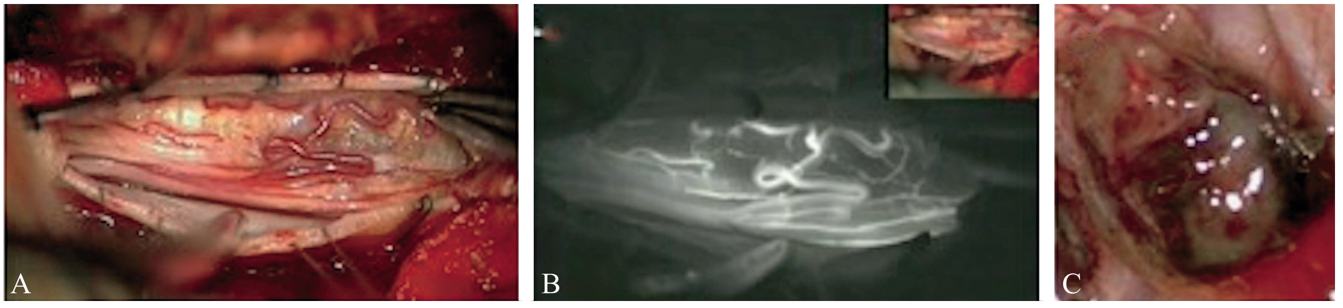

Figure 2.—A) Intraoperative photograph shows the exposure for resection of a SCM; B) intraoperative indocyanine green angiography of SCM; C) macroscopic image of an extirpated SCM.

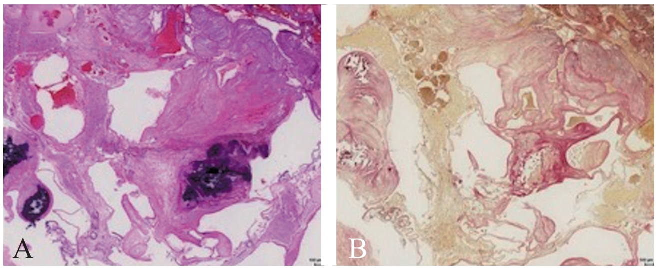

Figure 3.—A) Photomicrograph showing closely apposed thickened, hyalinized vascular channels without intervening neural tissue. The vascular channels lack an elastic lamina (B, elastica van Gieson stain). The edge of the lesion shows evidence of old hemorrhage, gliosis and calcification. (Courtesy of Prof. Elisabeth Rushing Department of Neuropathology University Hospital Zurich, Zurich, Switzerland).

carried out to determine the location and size of dura incision (Figures 5, 6). In some cases repeated imaging was used after initial small myelotomy to assure exact positioning above the CM before further deeper incision. No corrections of myelotomy was performed because of exact anatomical localization by the high frequency ultrasound probe.

After resection high frequency probes were also used for resection control. In patients with short durations of symptoms prior to surgery and associated edema, resection control was more difficult to interpret (Figure 6, case #1; operative group) compared to patients with a longer period of symptoms and mild perilesional edema (Figure 5, case #20; operative group).

Postoperative course and final evaluation

Surgical group

Preoperative Frankel score was grade E in 3 (14, 3%), grade D in 15 (71.4%), grade C in 2 (9.5%) and grade A in 1 patient (4.8%) in the surgical group (Table III). Six patients (28.6%) experienced in the immediate postoperative

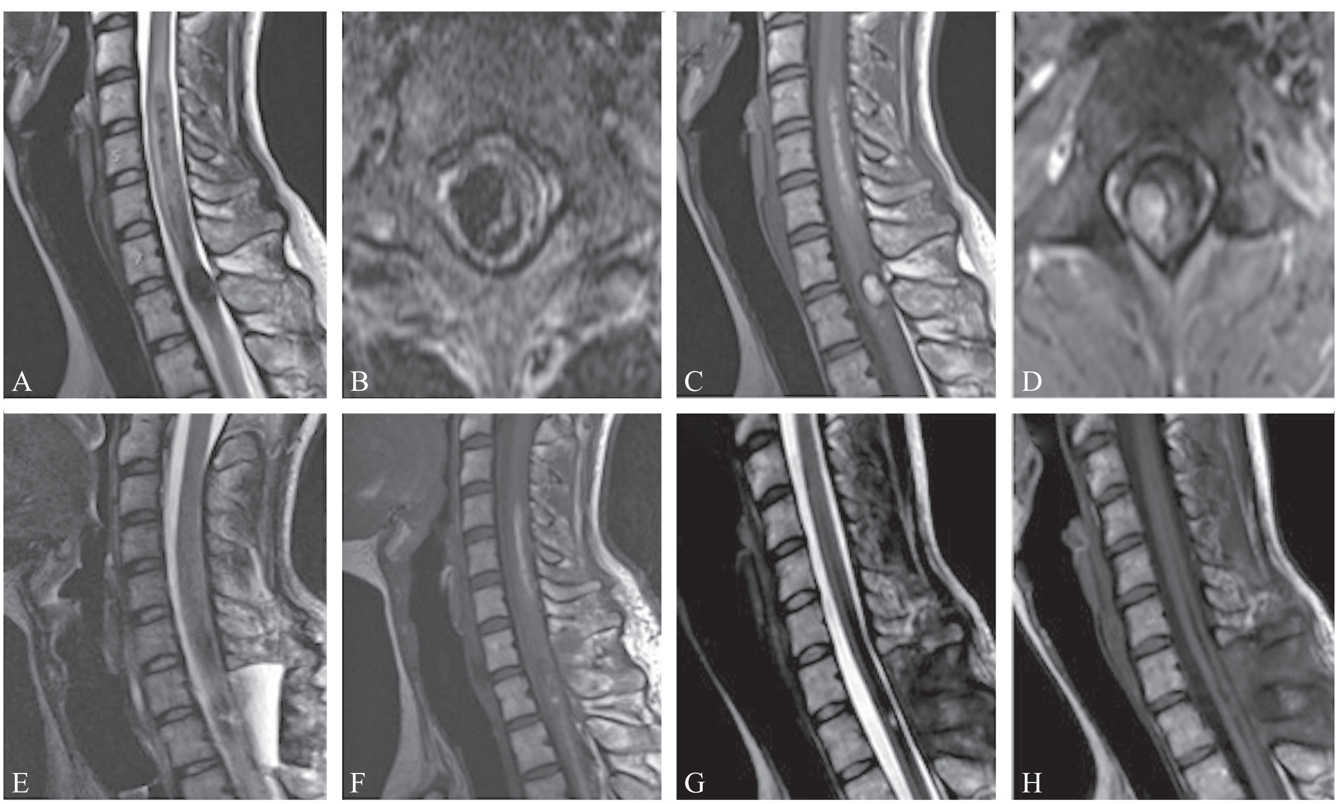

Figure 4.—Preoperative sagittal (A) and axial (B) native T2-weighted MRI of a 30-year-old patient with SCM at the level of C7-T1 (case #2; operative group). Sagittal (C) and axial (D) T1-weighted preoperative MRI. The patient underwent a right unilateral laminectomy of C7-T1 and extirpation of the lesion. Intraoperative MRI reveals complete removal of SCM (E, F); three months after surgery, the MR images show no residue or recurrence of the SCM (G, H) (E and G are sagittal T2-weighted images; F and H are sagittal T2-weighted; panels F and H are sagittal T1-weighted images).

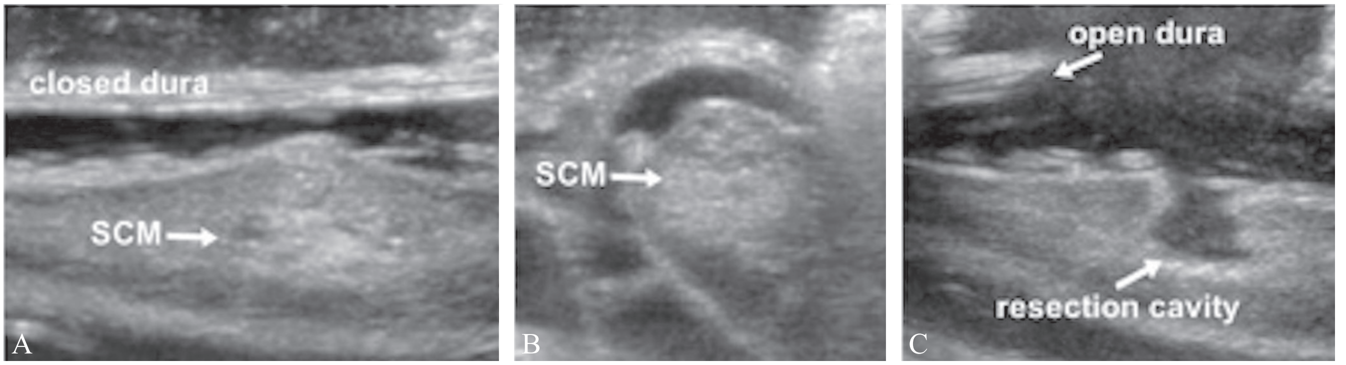

Figure 5.—A 46-year-old woman with an SCM at the level of C2 -3 (case #20; operative group) sagittal (A, C) and axial (B) intraoperative high frequency ultrasound. The patient showed subacute symptoms (1 month) and underwent a right unilateral lamincetomy of C 3 and extirpation of the lesion.

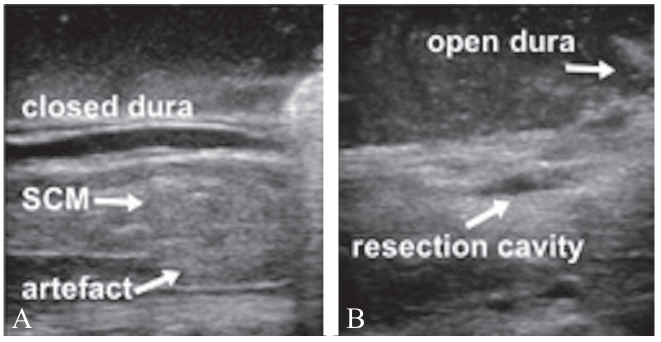

Figure 6.—A 32-year-old woman with a SCM at the level of T 9 (case #1; operative group) intraoperative high frequency ultrasound (A) SCM before dura opening (B). The resection cavity with open dura. The accurate differentiation of medullary to possible residual pathological tissue is hindered due to perifocal edema. The patient presented with acute symptoms (3 days) and underwent a left unilateral laminectomy of T 9 and extirpation of the lesion.

course a transient deterioration of the neurological function, whereas in only 3 patients (14.3%) the neurological function was categorized worse by 1 Frankel grade. Two patients (9.5%) experienced immediate improvement of the preexisting neurological deficits and improved by 1 Frankel grade. Postoperative Frankel score was grade E in 1 (4.8%), grade D in 17 (80.1%), grade C in 2 (9.5%) and grade B in 1 patient (5.6%) at discharge. There was no cerebrospinal fluid (CSF) leak, no postoperative bleeding or operative mortality. 2 patients experienced wound infection in our patient cohort.

Surgically treated patients were examined for the first follow-up after 3-6 months. During short-time follow-up (3-6 months) Frankel score was grade E in 8 (38.1%), grade D in 12 (57.1%) and grade C in 1 patient (4.7%). Thus, 61.9% of them (N.=13) remained unchanged compared to their preoperative status, while 33.1% (N.=7) improved and only 4.8% (N.=1 patient) worsened during short time follow-up.

At last follow-up evaluation, functional status had improved in 15 patients (62.5%) and remained unchanged in 6 patients (28.5%). One patient (case #7) reported of a remaining allodynia of the right upper limb after the operation, while no clinical abnormalities in sensory or motor function could be detected. No patient showed a deterioration of the preexisting neurological deficit during long-term follow-up. The immediate and long- term neurological outcomes after surgery are reported in Table III.

Conservative group

In the present series 8 patients (27.6%) were managed conservatively. At the time of diagnosis Frankel score was grade E in 5 (62, 5%), grade D in 2 (20.5%) and grade C in 1 patient (12.5%). During short-term follow-up (3-6 m) 1 patient experienced improvement of the preexisting neurological deficit, whereas 7 patients remained unchanged. During long-term follow-up 2 patients (25%) improved and 6 patients (75%) remained unchanged (Table IV).

Discussion

Epidemiological and clinical features

SCM are rare entities but with the broad use of modern imaging techniques the incidence of SCM has significantly increased over the last decades — especially due to incidental findings in patients undergoing spinal imaging for evaluation of degenerative conditions. SCM previously accounted for 5-12% of all lesions in the spinal cord.[28] To date, SCM account for up to 20% of intramedullary spinal cord tumors in adults.[2] As many as 40% of patients with SCM may harbor CCM.[7, 8] In our patient cohort only 2 patients (6.8%) had a known CCM pathology — of note, cMRI was performed in only 13 patients (44.8%); while no cMRI was available in 16 patients (55.2%). In comparison with CCM, SCM are thought to result in worse outcomes.[29, 30] SCM occur most often in the thoracic (55%) followed by the cervical (38%) and lumbar spine[4, 31] — in accordance with this data the location of the CM within the spine was cervical in 10 (34.5%), cervicothoracic in 3 (10.4%) and thoracic in 16 patients (55.2%) in our patient cohort. In adults, no sex predominance has been described.[3, 4] There was a slightly female dominance (N.=16, 55.2%) in our patient cohort. The mean patient age in our patient cohort was 44.6 years (range 13.8-81.5 years) in accordance with previously published data.[3, 4] The hemorrhage rate per year of SCM reported in the literature various from 1.4% to 6.8%.[6, 8, 10, 12, 29, 32-35] There is a high heterogeneity in the cited hemorrhage rates due to the variable definitions of hemorrhage among the studies. According to Badhiwala *et al.*[4] the calculated pooled estimate of the annual rate of SCM hemorrhage is 2.1%.

Clinical presentation is distinct but most often occurs with acute onset of neurological deficits due to intramedullary hemorrhage. Most patient present with sensory or motor deficit (about 60% of the cases respectively), followed by pain (34%) and bladder/bowel dysfunction (24%).[4]

Ogilvy *et al.*[36] previously reported 5 types of pattern of clinical presentation:

- type I: discrete and acute onset of symptoms over a period of months to years followed by a decline of neurological deficits, caused by intermittent rebleeding and various degrees of recovery;
- type II: slow, progressive decline of neurological symptoms, likely caused by intermittend rebleeding with progressive enlargement of the lesion;
- type III: acute onset of symptoms followed by rapid decline in neurological functions, caused by macrohemorrhage forming a space-occupying lesion;
- type IV acute onset of mild symptoms followed by a gradually progressive decline in neurological function as the result of recurrent hemorrhage;
- type V: sudden onset of back pain with or without neurological deficits due to subarachnoid hemorrhage from superficially located SCM.[14, 25, 37]

Clinical imaging used for cavernoma management-diagnosis, preoperative, postoperative

CM are described as angiographically occult due to the minimal blood flow in these lesions.[38] Thus, other imaging techniques are essential to provide an accurate diagnosis. Conventional T1- and T2-weighted MR imaging, gradient echo sequences, as well as susceptibility- weighted imaging is the gold standard for imaging diagnosis of CM.

On T2-weighted MRI CM show a pathognomic image which includes a peripheral ring of hemosiderin deposition due to repeated micro-hemorrhages (Figure 1).[39, 40] The specify and sensitivity of conventional MRI sequences (T1- and T2 weighted imaging) is nearing 100%.[41] T2*-weighted GRE have been shown to be more sensitive than conventional sequences due to its ability to display areas containing hemosiderin-laden tissue with a more recognizable hypointensity on T2 weighted images.[42, 43] Four types of CM may be differentiated based on their appearance on MR imaging.

- type I lesions are characterized by hyperintensity on T1- and T2-weighted imaging due to a hemosiderin core from subacute hemorrhage;
- type II lesions contain loculated regions of hemorrhage surrounded by gliotic tissue, presenting with mixed-signal intensity on both T1 and T2 sequences. On T2 imaging, type II these lesions exhibit a hypointense rim, resulting in the "popcorn" appearance;[40, 44]
- type III lesions are diagnosed by the presence of an iso- or hypointense core, compatible with chronic resolved hemorrhage, typically seen in familial CM;
- type IV lesions are minute lesions that can only be seen in gradient recalled echo (GRE). These lesions harbor a hypointense foci and are thought to be capillary telangiectasias or early stages CCMs seen frequently in familial CCM.[40, 43, 45]

Indication and timing of surgery

According to the available literature surgical resection can be considered in all patients with symptomatic lesions.[4, 10, 25, 21, 14, 46, 47] Operative risks in this highly eloquent tissue need to be fully disclosed to the patient and patients should be referred to a neurosurgical department with great expertise on the field of SCM.[21, 46, 47]

Surgical extirpation of the lesion can be considered for progressively enlarging lesions or in cases of recurrent hemorrhages. In young patients with mild symptoms final treatment decision is difficult.[4, 25, 18] In addition, one has to bear in mind that due to the confined space where SCM are located, the risk of significant morbidity after a bleeding episode is considerable. Furthermore, an average hemorrhage rate per year of 2.1% has to be considered, especially in young patients.[4] In general, spinal cord surgery has become safer during the last decade, especially due to recent introduction of intraoperative neurophysiological monitoring (IONM).[18, 14, 48] SCM resection can safely be completed when D-Wave is stable in IONM, assuring the functional integrity of the spinal cord motor tracts during surgery.[22, 23, 49]

The perfect timing for surgical intervention in patients with SCM is controversial. Early surgical intervention is recommended for a better surgical outcome —[4, 32] Steiger *et al.*[11] showed that the postoperative course is unsatisfactory in patients with a long history of symptoms. Badhiwala *et al.*[4] recommend surgical intervention within 3 months of presentation on the basis of a statistically significant correlation between shorter duration of presurgical symptoms (≤3 months) and favorable clinical outcome. Whereas Imagama *et al.*[19] propose to postpone surgery until patients recover from preoperative motor paresis to allow best surgical outcome.[4, 19] Imagama *et al.*[19] showed that patients with preoperative stable gait were significantly more likely to have a postoperative stable gait. They recommend early surgery before long disease duration for asymptomatic patients with a thoracic or large tumor showing stable gait without significant motor paresis.

Our strategy is to extirpate the SCM lesion on an early basis after symptomatic hemorrhage to prevent neurological deterioration due to recurrent hemorrhage.

In accordance with the findings of Jallo *et al.*,[3] we confirm, that the neurological decline due to chronic myelopathy is not as reversible as the acute presentation.

Surgery associated/immediate surgical complications

Mitha *et al.*[14] described in their series with 80 surgical treated patients with SCM immediate surgical complications in 5 patients (6%) — CSF leak and deep venous thrombosis were the most common occurrences in the early postoperative period. Furthermore Mitha *et al.*[14] reported, that compared with their preoperative status, the immediate neurological outcome of 9 patients (11%) was worse by 1 Frankel grade. In our patient cohort there was no CSF leak, no postoperative bleeding or operative mortality. Immediately after surgery, 6 patients (28.6%) had a transient deterioration of the neurological function, whereas in only 3 patients (14.3%) transient deterioration of the neurological function led to a downgrade in Frankel Scale (Table III). New neurological deficits were predominantly paresis, hypoesthesia, and neuropathic pain. One out of the 6 patients, who experienced a transient deterioration of the of neurological function was diagnosed with Brown Séquard syndrome. Nevertheless, during long-term follow-up no patient showed a deterioration of the preexisting neurological deficit. In the postoperative course 2 patients experienced wound infection in our patient cohort.

Late surgical complications

Mitha *et al.*[14] described in their series with 80 surgical treated patients with SCM delayed surgical complications in 14% of patients – post laminectomy kyposis was the most common delayed surgical complication. No statistically significant difference in the occurrence of kyphosis between each type of procedure (laminectomy *vs*. laminoplasty) was detected.[14] Symptomatic cervical stenosis involving the surgical site and new symptoms related to spinal cord tethering at the surgical site displayed late surgical complications as well.[14] In our patient cohort 3 patients (14.2%) showed late surgical complications. One patient, a 14-year old boy, experienced post laminectomy kyposis with progressive cervical myelopathy and had to undergo correction of kyphosis using ventral discectomy and fusion of C3-C6. Hypertrophic scarring led to revision surgery in one case. Furthermore, one patient experienced pronounced neuropathic pain.

Conservative management

The natural history of SCM is mainly unknown due to the relatively small number of conservatively managed patients reported in the literature. Among all published studies, only in 10% of the patients with SCM treatment was conservative management by observation,[4, 46] reflecting the general practice among neurosurgeons of resecting SCM when patients are symptomatic. According to the literature in asymptomatic patients follow-up should be performed, while in otherwise healthy, symptomatic patients surgery is generally safe and recommended.[4, 11, 13, 14, 18] No clinical trial, in which patients with SCM are randomly assigned to either surgical or medical management has been published so far. Furthermore, no larger retrospective study which documents the natural history of SCM has been published. Only few retrospectively studied patients who did not receive surgical treatment for various reasons have been described in the literature.[4, 9, 11, 13, 18] Previous studies regarding SCM have been largely limited to surgically managed patients from a small number of tertiary care centers focusing on the surgical approach and techniques. Badhiwala *et al.*[4] outline, that prolonged observation of symptomatic lesions is likely to lead to progressive clinical decline resulting in worse patient outcome. In an international meta-analysis Badhiwala *et al.*[4] showed that the rates of improved, stable, and declined neurological function among patients who underwent conservative management were 30%, 58%, and 11% respectively, whereas in comparison, neurological outcomes among patients who underwent surgery was improved in 51%, unchanged in 38% and worse in 11%.[4]

In the present study 8 patients (27.6%) were managed conservatively. The majority of these patients showed a stable condition (75%) with unchanged neurological function during long-term follow-up (median follow-up 3.2 (±0.58) years per patient; range 0.4-10.4 years). Two patients (25%) even improved during long-term follow-up. Thus we advocate, that conservative treatment is a safe option if initial symptoms are mild and do not show progression over time. Indication for surgical extirpation of an SCM lesion should be decided with caution in elderly patients. Figure 8 shows a representative case.

Intraoperative neurophysiological monitoring

IONM has become a standard tool in spinal cord surgery (Figure 8)[50, 51] and has contributed to reduction of postoperative morbidity.[13, 52] At our institution, we routinely monitor somatosensory evoked potentials (SSEPs), muscle motor evoked potentials (muscle MEPs), and – for cervical and thoracic lesions- spinal motor evoked potentials (spinal MEPs; also called "D-wave"). Liang *et al.*[13] reported in their series, that four out of five patients who worsened after surgery of SCM were operated in the era before intraoperative SEP and MEP monitoring.

Among the modalities of IONM, SSEP, with excellent ability to assess dorsal column and lateral sensory tract function, is the standard for intramedullary SCM surgery, since intramedullary SCM are normally located at the dorsal surface of spinal cord.[22, 23] In our case series, we did not find a false negative result, *i.e.* a patient in whom a postoperative neurological deficit occurred in spite of unchanged SSEP. Nevertheless, for intramedullary spinal tumor resection, SEPs should be used in combination with

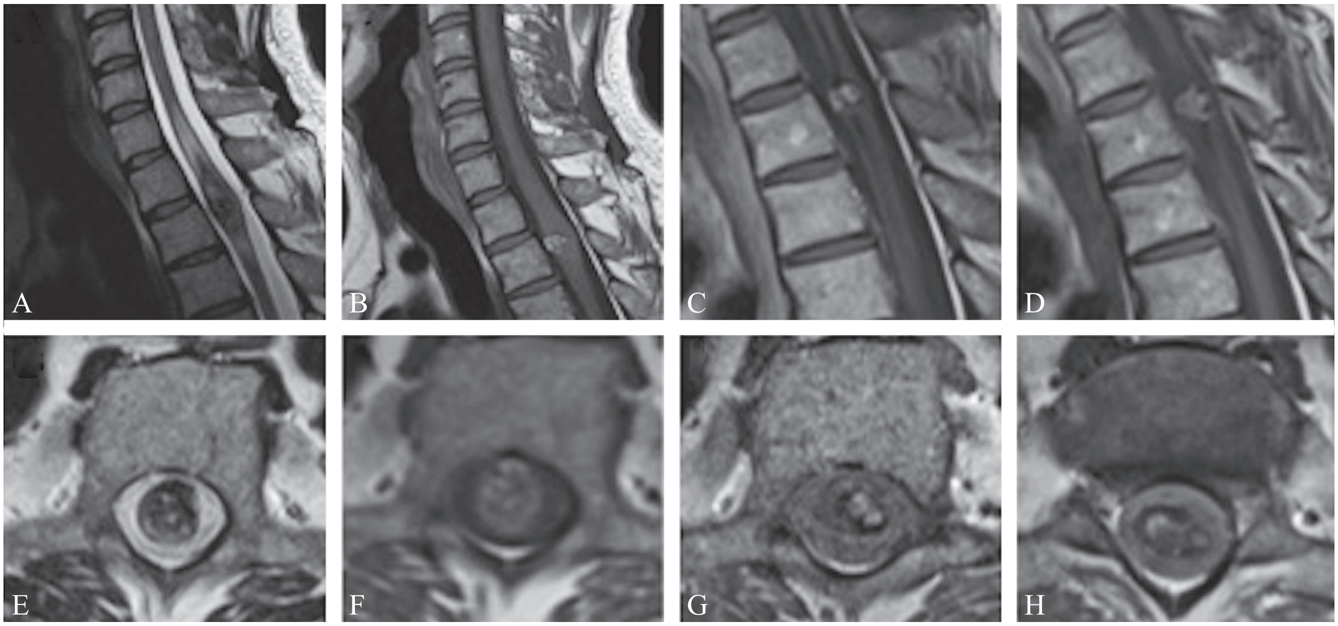

Figure 7.—A 47-year-old patient with an SCM at the level of T 2 (case #5, conservative group). The patient presented with motor deficit of his left leg since one week. Sagittal (A) and axial (E) native T2-weighted and sagittal (B) and axial (F) T1-weighted MRI at diagnosis showing the SCM at level T 2. Follow-up MRI after 3 months (C, G) and 1 year (D, H) shows stable conditions. C and D are sagittal T1-weighted; G and H are axial T1-weighted images.

MEPs. The modalities to monitor the functional integrity of the descending corticospinal tract are MEP and D-wave recordings. In both modalities, the motor cortex is stimulated transcranially. MEP responses are recorded preferentially from distal muscles of the hand and the foot. For D-wave recordings, an epidural catheter is placed in the field of surgery.

While muscle MEP monitoring seems to be an adequate method for monitoring the functional integrity of the corticospinal tract during most spine surgeries, for intramedullary spinal cord tumor surgery muscle MEP have to be carefully interpreted. In well documented studies on more than 100 intramedullary spinal cord tumor surgeries, it has been shown that a preserved D wave up to 50% of the original amplitude, with a complete loss of muscle MEPs, results in only transient paraplegia.[22-24] Thus, despite previously published data, the complete disappearance of muscle MEPs is acceptable, if monitoring for intramedullary tumors is done with both D waves and muscle MEPs.[22-24] Beside the standardized use of SEPs and muscle MEPs, D-wave recording is an essential to monitor the functional integrity of the descending corticospinal tract. D-wave changes — when recordable — have proven to be the strongest predictors of maintained corticospinal tract integrity (and therefore, of motor function/recovery).[49] Morota *et al.*[53] reported, that patients who lose the D wave during spinal cord surgery usually become permanently paraplegic.

Combining the use of muscle MEPs with D-wave recordings provides the most comprehensive approach for assessing the functional integrity of the spinal cord motor tracts during surgery for intramedullary spinal cord tumors.[49]

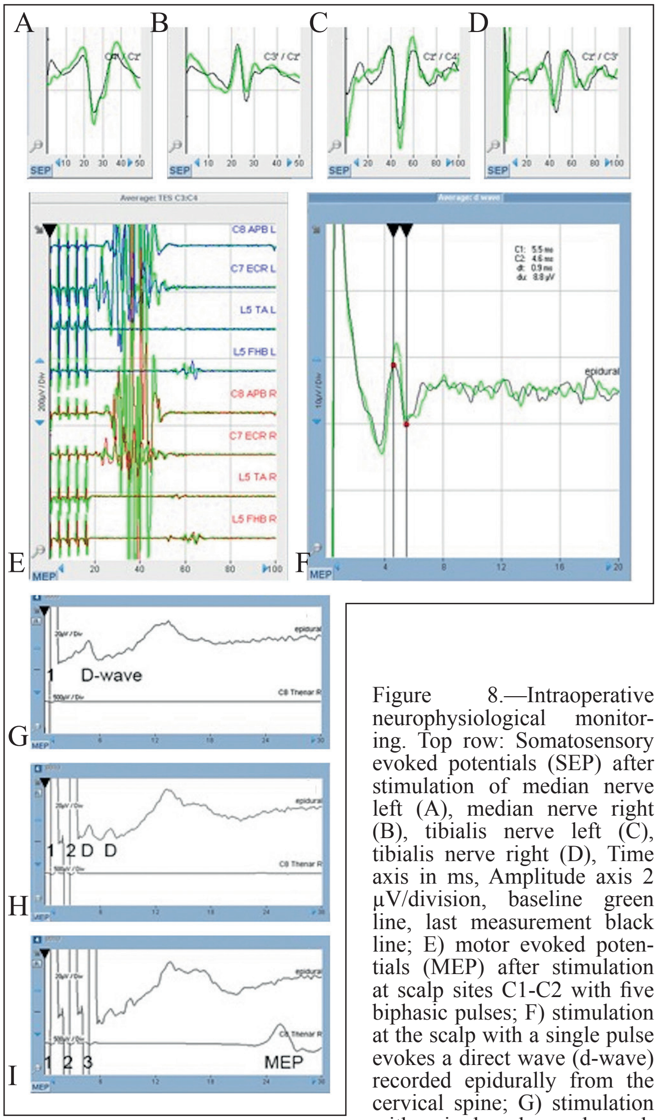

Figure 8.—Intraoperative neurophysiological monitoring. Top row: Somatosensory evoked potentials (SEP) after stimulation of median nerve left (A), median nerve right (B), tibialis nerve left (C), tibialis nerve right (D), Time axis in ms, Amplitude axis 2 µV/division, baseline green line, last measurement black line; E) motor evoked potentials (MEP) after stimulation at scalp sites C1-C2 with five biphasic pulses; F) stimulation at the scalp with a single pulse evokes a direct wave (d-wave) recorded epidurally from the cervical spine; G) stimulation with a single pulse evokes a d-wave at 4 ms and muscular response at 12 ms but no response below the lower motor neuron at the thenar muscles; H) two pulses evoke two d-waves; I) stimulation at the scalp with three pulses evokes an MEP at 26 ms from the thenar muscles.

Surgical procedure

With regard to surgical approaches, unilateral laminectomy is associated with better outcomes compared to total laminectomy or laminoplasty.[4] However, unilateral laminectomy in young patients may lead to scoliosis, in those cases laminoplasty is preferred at our department. Unilateral laminectomy should be performed over the appropriate spinal level. SCM are typically located posteriorly in the midline. In these cases SCM are often visually localized as an exophytic lesion, blue-purple discoloration, and/or bulging of the dorsal pial surface (Figure 3).

Mitha *et al.* described in 2011 3 primary operative approaches to SCM: posterior, posterolateral, and lateral.[14] Posterior midline myelotomy is the most common approach — due to the typically location of SCM posteriorly in the midline,[14] anterior approaches to the spinal cord significantly raises the risks of ischemia/infarction. It is not unfrequent for SCM to be visible on the surface — in this cases we advise to use this as the approach entry zone and perform the myelotomy in this area.

Myelotomy should be performed as small and as precise as possible to gain an excellent exposure on the one hand and to avoid retraction on the other hand.[14, 20]

SCM should be removed completely while the hemosiderin rim attached to the surrounding neuronal tissue should be preserved. Associated venous malformations drain normal tissue and must be preserved — removing the DVA entails a high risk of venous infarction.[54]

Once the lesion has been removed, the operative cavity must be carefully examined to identify any residual SCM. High definition ultrasound is highly recommend for resection control.[20] Complete removal of the lesion is essential to prevent recurrent hemorrhage — nevertheless, we showed previously that the outcome depends on the neurosurgeon's expertise.[21] Rebleeding occurs in up to 40% of CM remnants after surgery,[55] which is why postoperative MRI is highly recommended within 72 hours after surgery. In case of remnants, surgical intervention should be performed on an early basis.[55]

Intraoperative ultrasound

In order to facilitate the intramedullary localization of the SCM, intraoperative high definition ultrasound is recommended before opening the dura.[56] There is practically no alternative to intraoperative ultrasound (ioUS) to locate the SCM after opening the spinal canal. We previously showed, that high frequency ioUS is the best choice before and after opening the dura, or even after initial myelotomy for intraoperative imaging to localize and to visualize SCM and to keep the spinal cord incision as small and as precise as possible.[20] In addition, high frequency ioUS is very well suitable for intraoperative resection control of SCM lesions with little edema and non-recent hemorrhage. Interpretation of ioUS in SCM with perifocal edema or hemosiderin needs great expertise in the field of ioUS and accurate differentiation of medullary to pathological tissue might be difficult (Figure 6).[20]

Outcome

The outcome of surgical intervention depends on the institutional and the surgeon's experience and a well-established indication for treatment. Of 26 patients reported by Jallo *et al.*[3] neurological status improved immediately after surgery in 20%, remained clinically unchanged in 30%, and decreased in 50%, whereas during long-term follow-up 46% of the patients improved, 46% of the patients remained unchanged and 8% of the patients worsened (mean follow-up 4.5 years; range 4 months - 10 years). Liang *et al.*[13] reported, that at the end of the follow-up period (mean follow-up 3.8 years; range 10 months - 15 years) in the operative group, 23 patients (36%) improved, 35 patients (55%) remained unchanged, and 6 patients (9%) worsened.

Badhiwala *et al.*[4] showed that gross-total resection correlates with a significant improvement for overall outcome — for patients for whom gross-total resection was achieved. Rates of good, fair, and poor out comes were good in 60%, fair in 32% and poor in 8%, whereas 29%, 47%, 24% for patients for whom resection was incomplete (biopsy, partial, or subtotal); and 32%, 55%, 13% for patients who underwent conservative management. Therefore postoperative MRI displays an essential adjunct to identify residual cavernoma (Figure 4). An initial pattern of acute/stepwise rather than slowly progressive clinical presentation is associated with a better neurological function at follow-up.[4]

During short-term follow-up (3-6 months) 61.9% (N.=13) remained unchanged in our operative patient cohort compared to their preoperative status, while 33.3 (N.=7) improved and only 4.8% (N.=1 patients) worsened. During long-term follow-up (3.2±0.58 years), functional status had improved in 15 patients (62. 5%) and remained unchanged in 6 patients (28.5%). No patient showed a deterioration of the preexisting neurological deficit in our patient cohort during long-term follow-up.

Among the conservatively treated patients in the present study two patients experienced improvement of the preexisting neurological deficit, whereas 1 patient remained unchanged during short-term follow-up (3-6 months). During long-term follow-up (3.2±0.58 years), 2 patients (25%) improved, whereas 6 patients (75%) remained unchanged.

Thus, in our experience patients with severe neurological deficits due to SCM bleeding benefit from surgical extirpation of the SCM lesion and surgical extirpation of the SCM can be performed with an acceptable risk of complications. Complete resection of symptomatic intramedullary SCM should be performed to prevent further neurological decline. Furthermore the results of this study outline that in patients with mild symptoms conservative treatment seems to be an options as well — acute deterioration with severe neurological deficits is rare and did not occur in our patient cohort. According to the literature, we confirm that improved outcome is more often observed in surgically treated patients with SCM.

Limitations of the study

Limitations of our study are: 1) a potential selection bias since patients with asymptomatic lesions or a poor preoperative functional status might not have been brought to our attention; and 2) the retrospective study design of our own series but also of most published series. A prospective multicenter randomized study or a registry for patients with SCM is highly recommended, however funding will be very challenging. Institutions should combine their patient data to one registry and achieve one profound consensus thereby.

Conclusions

Resection is the only definitive treatment option for symptomatic SCM.

Gross-total resection through a more minimally invasive unilateral laminectomy approach within 3 months of presentation is recommended for symptomatic SCM with good long-term outcomes and with an acceptable risk of complications.

Conservative treatment should be performed in asymptomatic patients and seems to be an option as well in elderly patients and if patients' symptoms at diagnosis are mild and do not show progression over time.

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